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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,105	02/27/2004	Claire Trelford Roberts	LP-02-019	7714

7590 12/29/2005

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,105	ROBERTS ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-7, drawn to method of regulating cytotrophoblast differentiation and migration and/or promoting embryo implantation in the uterine decidual endometrium, comprising administration of IGF-II in the reply filed on 5 October 2005 is acknowledged. Claims 8-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election ***without*** traverse (MPEP § 818.03(a)).

Oath

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because the continuing and foreign priority data are incorrect. This application is not a continuation of PCT/AU02/01226, but rather it claims benefit of priority to PCT/AU02/01226. A petition was granted under 37 CFR 1.78(a)(3) filed November 23, 2005, to accept an unintentionally delayed claim under 35 U.S.C. 120 for the benefit of priority to the prior-filed International Application No. PCT/AU02/01226 filed August 30, 2002.

Claim Rejections - 35 USC § 112 – second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph because the method steps fail to achieve the goal set forth in the preamble. In claim 1, the "method of regulating cytorophoblast differentiation and migration comprising regulating the competition for binding to the CIM6P receptor between IGF-II and latent TGF-β" is not incorporated into the method steps recited in the claim. Likewise, in claim 2, method of promoting the implantation of an embryo in the uterine decidual endometrium, the method comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β is not incorporated into the method steps recited in the claim. Therefore, it is unclear if the claims are directed to methods of regulating cytotrophoblast differentiation and migration or methods of regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and TGFβ.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2 (and 3-7, which depend from claim 2 and incorporate all its limitations) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The stated intention of the methods of claims 1 and 2 is to regulate cytotrophoblast differentiation and migration (claim 1) and to promote the implantation of an embryo in the uterine decidual endometrium (claim 2), the methods comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β, however, these statements are ***totally non-enabled***. Evidence is presented on p. 22, lines 21-34 of the specification that "treatment of pregnant mice between days 2 and 10 of pregnancy increased placental weight at day 18 of gestation by 7.5% ($p<0.05$) and 9.6% ($p<0.05$) by treatment with 12.5 or 25 μg/day IGF-II, respectively (FIG. 5). The percentage of placentas that weighed more than 120 mg was 3.1% in control mice, 25.8% in mice treated with the 12.5 μg/day IGF-II, ($p<0.0001$) and 29.8% in mice treated with the 25 μg/day IGF-II ($p<0.0001$) (FIG. 6). Thus treatment of the dam with slow release IGF-II during the first half of pregnancy enhances placental growth. Treatment with 25 μg/day IGF-II increased fetal weight by 4.1% ($p<0.05$) (FIG. 7). The distribution of fetal weights across litters was skewed to the right by treatment with IGF-II. The percentage of fetuses weighing more than 1100 mg was 21.5% in control mice, 27.4% in mice treated with 12.5 μg/day IGF-II (NS) and 53.6% in mice treated with the 25 μg/day IGF-II ($p<0.0001$)

(FIG. 8)." However compelling the data are, they only suggest that treatment of IGF-II increase placental and birth weight, which is not necessarily due to regulation of cytotrophoblast differentiation and migration (claim 1) and promotion of embryo implantation in the uterine decidual endometrium (claim 2), comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β. Furthermore, Behr and Wang (Eur J Obstet Gynecol Reprod Biol. 2004; 115 Suppl 1:S72-6) note that not all manipulations in embryo culture are benign, and further report that in spite of growing evidence that growth factors may be important in a variety of mammalian species in pre-implantation development and cell signaling, caution is warranted (see especially p. s73, columns 1 and 2, section 4 on Growth factors and preimplantation development).

Due to the large quantity of experimentation necessary to determine the appropriate culture conditions for human, horse, cow, pig goat and sheep embryos to achieve regulation of cytotrophoblast differentiation and migration and promotion of the implantation of an embryo in the uterine decidual endometrium, comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β, the lack of direction/guidance presented in the specification regarding these limitations, the absence of working examples directed to these limitations and to treatment of higher mammals with IGF-II, the complex nature of the invention, the state of the prior art (see Behr and Wang, who discuss culture conditions for IVF) and the unpredictability of the effects of cytokine administration in different species during embryo development (again, see Behr and Wang), undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 3, 4, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by C. O'Neill (Biol. Reprod. 56:229-237, 1997). O'Neill teaches a method of administration of IGF-II to mouse embryos while maintaining the embryos in a relatively hypoxic environment (for oxygen conditions, see p. 231, column 1, 4th paragraph under the subheading Oxygen Tension; for method of administration of IGF-II, see especially, p. 234, Table 6).

Claims 1, 2, 4, 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Gluckman et al. (Patent # 5,420,111). Gluckman et al. teach a method of administration of IGF-II to a pregnant female (see column 3, lines 47-51) at "any time from conception forward." Furthermore, in column 8, line 34-51, the methods are envisioned as having industrial applicability in human medicine and farm animals.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over O'Neill (Biol Reprod, 1997—see above). As stated above, O'Neill teaches a method of administration of IGF-II to mouse embryos while maintaining the embryos in a relatively hypoxic environment. O'Neill does not teach treatment of human, horse, cow, pig, goat or sheep embryos. However, O'Neil implies that the results have applicability to other mammals, including human (p. 235, column 1, 2nd paragraph). Therefore, it would have been obvious to one of ordinary skill in the art to modify the method of O'Neill by administering IGF-II to human patients with a reasonable expectation of success. The motivation to do so is found in O'Neill's indication that such would increase implantation

and viability rates following embryo transfer, and one would expect success because of the increased stimulation of embryo development that occurred using O'Neill's methods (see Discussion, esp. p. 236, column 1, 3rd paragraph).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christina Borgeest, Ph.D.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER